

Amendments to the Claims:

The following listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

- 1.-17. (canceled)
18. (new) A chemically synthesized doubled stranded micro-RNA (miRNA) molecule, wherein:
  - (a) each strand of said miRNA molecule is 19 to 29 nucleotides in length;
  - (b) one strand of said miRNA molecule comprises a nucleotide sequence having complementarity to a target RNA;
  - (c) at least 20% of the internal nucleotides of said miRNA molecule are modified nucleosides; and
  - (d) at least two of said modifications are different from each other.
19. (new) The miRNA molecule of claim 18, wherein said miRNA molecule comprises no ribonucleotides.
20. (new) The miRNA molecule of claim 18, wherein said miRNA molecule comprises ribonucleotides.
21. (new) The miRNA molecule of claim 18, wherein each strand of the miRNA molecule comprises 19 to 29 nucleotides, and wherein each strand comprises at least 19 nucleotides that are complementary to the nucleotides of the other strand.
22. (new) The miRNA molecule of claim 18, wherein each strand comprises 19 to 29 nucleotides, and wherein one strand comprises at least 19 nucleotides that are complementary to nucleotides of the other region.
23. (new) The miRNA molecule of claim 22, wherein said miRNA molecule is assembled from two separate oligonucleotide fragments wherein one fragment comprises the sense region and the second fragment comprises the antisense region of said miRNA molecule.

24. (new) The miRNA molecule of claim 22, wherein said sense region is connected to the antisense region via a linker molecule.
25. (new) The miRNA molecule of claim 24, wherein said linker molecule is a polynucleotide linker.
26. (new) The miRNA molecule of claim 24, wherein said linker molecule is a non-nucleotide linker.
27. (new) The miRNA molecule of claim 22, wherein pyrimidine nucleotides in the sense region are 2'-O-methyl pyrimidine nucleotides.
28. (new) The miRNA molecule of claim 22, wherein purine nucleotides in the sense region are 2'-deoxy purine nucleotides.
29. (new) The miRNA molecule of claim 22, wherein the pyrimidine nucleotides present in the sense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
30. (new) The miRNA molecule of claim 23, wherein the fragment comprising said sense region includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends of the fragment comprising said sense region.
31. (new) The miRNA molecule of claim 61, wherein said terminal cap moiety is an inverted deoxy abasic moiety.
32. (new) The miRNA molecule of claim 53, wherein the pyrimidine nucleotides of said antisense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
33. (new) The miRNA molecule of claim 53, wherein the purine nucleotides of said antisense region are 2'-O-methyl purine nucleotides.
34. (new) The miRNA molecule of claim 53, wherein the purine nucleotides present in said antisense region comprise 2'-deoxy- purine nucleotides.
35. (new) The miRNA molecule of claim 34, wherein said antisense region comprises a phosphorothioate internucleotide linkage at the 3' end of said antisense region.

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36. (new) The miRNA molecule of claim 22, wherein said antisense region comprises a glyceryl modification at the 3' end of said antisense region.
37. (new) The miRNA molecule of claim 23, wherein each of the two fragments of said miRNA molecule comprise 21 nucleotides.
38. (new) The miRNA molecule of claim 18, wherein 19 nucleotides of each fragment of the miRNA molecule are base-paired to the complementary nucleotides of the other fragment of the miRNA molecule and wherein at least two 3' terminal nucleotides of each fragment of the miRNA molecule are not base-paired to the nucleotides of the other fragment of the miRNA molecule.
39. (new) The miRNA molecule of claim 38, wherein each of the two 3' terminal nucleotides of each fragment of the miRNA molecule are 2'-deoxy-pyrimidines.
40. (new) The miRNA molecule of claim 39, wherein said 2'-deoxy-pyrimidine is 2'-deoxythymidine.
41. (new) The miRNA molecule of claim 37, wherein all 21 nucleotides of each fragment of the miRNA molecule are base-paired to the complementary nucleotides of the other fragment of the miRNA molecule.
42. (new) The miRNA molecule of claim 37, wherein 19 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a target gene or a portion thereof.
43. (new) The miRNA molecule of claim 37, wherein 21 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a target gene or a portion thereof.
44. (new) The miRNA molecule of claim 23, wherein the 5'-end of the fragment comprising said antisense region optionally includes a phosphate group.
45. (new) A pharmaceutical composition comprising the miRNA molecule of claim 18 in an acceptable carrier or diluent.

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46. (new) The miRNA molecule of claim 18, wherein, said modified nucleotide is a 2'-sugar modified nucleotide.
47. (new) The miRNA molecule of claim 46, wherein said 2'-sugar modification is selected from the group consisting of 2'-H, 2'-O-alkyl, 2'-O-CF<sub>3</sub> and 2'-deoxy-2'-fluoro.
48. (new) The miRNA of claim 18, wherein at least 30% of nucleotide positions in said miRNA molecule comprise modified nucleotides.
49. (new) The miRNA of claim 18, wherein at least 40% of nucleotide positions in said miRNA molecule comprise modified nucleotides.
50. (new) The miRNA of claim 18, wherein at least 50% of nucleotide positions in said miRNA molecule comprise modified nucleotides.
51. (new) The miRNA of claim 18, wherein said modified nucleotides are present in one strand or both strands of the miRNA molecule.

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